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(71) Applicant *(for all designated States except US)*: CAMBRIDGE CONSULTANTS LIMITED [GB/GB]; Science Park, Milton Road, Cambridge CB4 4DW (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: EASON, Stephen, William [GB/GB]; The Priory, Half Moon Lane, Redgrave, Diss, Norfolk IP22 1RX (GB). CLARKE, Roger, William [GB/GB]; 36 Parlour Close, Histon, Cambridgeshire CB4 4XP (GB). SARKAR, Matthew, Neil [GB/GB]; 33 Linden Close, Cambridge CB4 3JU (GB).

(74) Agent: DIXON, Philip, Matthew; Frank B. Dehn & Co., 179 Queen Victoria Street, London EC4V 4EL (GB).

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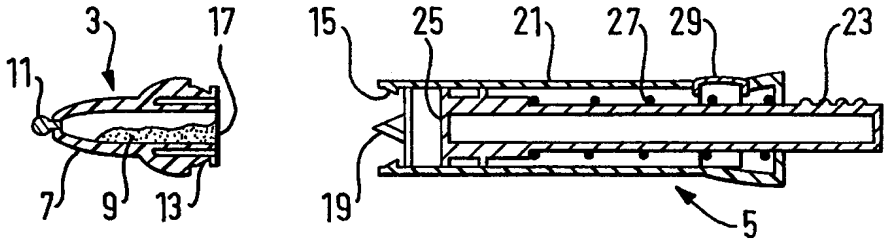


(57) Abstract

A drug delivery device (1) comprises a sealed capsule (3) for a single dose of a pharmaceutical (9). The capsule (3) is formed with a nozzle (7) for insertion into the nostril of a user so that the pharmaceutical (9) can be delivered into the nasal passages of the user. The capsule (3) connects to a holder (5) which optionally comprises a pump (23). After delivery of the pharmaceutical, the capsule (3) is disposed of so that all parts of the device that have contacted the nose are discarded and there is no need for cleaning.

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# Drug Delivery Device

The present invention relates to a drug delivery device and to a capsule therefor. In particular, the invention relates to a device for delivering a pharmaceutical preparation, for example in powder form, into an externally voiding cavity, such as the nasal passage, of a patient.

Devices to dispense medicines to the nasal passages have been known and used for many years. Devices dispensing liquids in a spray form are most common, but devices delivering powdered drugs are also known. Such devices are now becoming more relevant as a means of drug delivery, because innovations in drug technology mean that some drugs can only be formulated in a powdered form.

Devices which deliver powders to the nasal passages are traditionally of two types, both of which exhibit problems.

The first type of powder delivery device receives a single pre-packaged dose of the drug in a gelatine capsule. The gelatine capsule is placed inside the device, which has both a mechanism to pierce the capsule and an airway leading to a nozzle which can be placed in the nostril. The drug is delivered to the nasal passages either by patient inhalation, or by blowing air through the pierced capsule and out of the nozzle using a simple air pump incorporated into the device. In both cases the drug is entrained in the air stream and carried out of the device. Devices with a pump have the advantage that effective delivery is not dependent on the inhalation rate of the patient. An example of such a device is described in US Patent No. 3,949,751.

The powder delivery devices of the type described above exhibit the problem that they are complicated to

set up and use. The patient typically has to take the device apart, insert the capsule and then operate a piercing mechanism before being able to take the medicine. The spent capsule then has to be removed by separating the device again. Although an irritation for all patients, this process can be particularly difficult for some types of patient, such as children and the elderly, leading to incorrect usage or non-compliance with the dosing regime.

The second type of device attempts to solve this problem by containing within it a number of doses, such that the patient does not have to insert a new dose each time the device is used. In some devices, the doses are stored in a reservoir, for example as shown in U.S. Patent No. 5,702,362 and the device has a mechanism for metering each dose before use. Alternatively, the doses are stored as a number of pre-metered doses, for example as shown in US Patent No. 5,366,122. Both types of multiple-dose device require some action from the patient to set the device prior to use, but are still simpler to use than the single-dose device described previously.

However, multiple-dose devices exhibit a further problem in that they must adequately protect the stored, powdered drug from moisture or contamination. In the case of a single-dose device, the drug is protected in the gelatine capsule, but multiple dose devices typically do not protect the drug adequately, or resort to complex mechanical means to do so, resulting in a bulky and expensive device.

The problem of contamination and moisture is a problem with both types of device, since the nozzle of the device must be inserted into the nostril. Both the airway and external surfaces of the device are therefore prone to contamination by matter from the nose. This can lead to contamination of the drug where it is stored in the device. If the drug is prone to yeast or mould

growth this is clearly extremely undesirable.

If, as is sometimes recommended, the patient is required to clean the device by washing it in water the problem of moisture contamination arises. The potential for introducing moisture to the drug where it is stored in the device is clear, but for both types of device the patient must be careful to ensure that the airway is thoroughly dried before use. If not, the entrained powder will stick to the airway walls and the delivery efficiency will be impaired.

In view of the problems with known drug delivery devices, the present invention seeks to provide a new drug delivery device.

According to the present invention, there is provided a capsule comprising a single dose of a pharmaceutical sealed within the capsule, characterised in that the capsule further comprises a nozzle for delivery of the pharmaceutical.

Thus, according to the invention the nozzle forms part of the capsule which contains the drug and can be disposed of once the dose has been dispensed. In this way, there is no need to clean the nozzle after use, as it is simply thrown away, and there is therefore no possibility of the pharmaceutical being contaminated. Furthermore, the nozzle provides a convenient member with which the patient may grip the capsule in order to connect the capsule to a holder or pump.

The capsule is preferably arranged to be fitted to a holder to form a drug delivery device. The provision of a holder allows the capsule to be relatively small, for example only approximately the size of the nozzle, with the holder providing a larger component for the user to grip when guiding the nozzle into the nostril, once the capsule has been fitted to the holder.

Advantageously, the holder may be provided with means for penetrating the capsule to allow delivery of the pharmaceutical.

The capsule may be provided with a connector for connecting the capsule to the holder. The connector may be of any suitable type, for example a simple push-fit connector. Preferably, however, the connector is arranged to positively engage the holder so that the capsule is securely attached to the holder and will not easily be retained in the nostril when the holder is withdrawn. A bayonet-type connection or even a screw thread is suitable for this purpose. The capsule should be easily removable from the holder by the patient after use.

The capsule may be sealed by any suitable means. Preferably, the capsule is provided with a frangible seal which is penetrable by a member, such as a spike or the like, of the holder. Advantageously, the member is arranged to penetrate the frangible seal as the capsule is connected to the holder. The capsule may be provided with a plurality of frangible seals. In a particularly advantageous embodiment, the pharmaceutical may be located in the capsule between two frangible seals. The holder may be configured to break both frangible seals when the capsule is connected to the holder, so that the pharmaceutical can exit the capsule via the nozzle.

According to one particularly advantageous embodiment, the pharmaceutical is located in a passageway between two openings defined in the surface of the capsule, and each opening is closed by a frangible seal. Preferably, the openings are defined in the same surface of the capsule. In this case, the capsule can be filled through at least one of the openings and frangible seals may be formed by applying material, for example metal foil, over the opening(s). This provides a particularly simply filling method. Preferably, the openings are defined in a surface of the capsule which mates with a corresponding surface of the holder. In this way, the holder may be arranged to perforate the frangible seals. The holder may be

arranged to provide a communication channel between one of the openings and the nozzle when the capsule is connected to the holder. Such an arrangement allows both frangible seals to be on a holder-facing surface of the capsule so that they can both be perforated by respective members of the holder.

A valve or similar mechanism may be provided to close the nozzle and prevent contamination of the pharmaceutical before use. In one arrangement, however, sealing means are provided for sealing the nozzle. For example, a frangible seal may be provided across an opening of the nozzle which seal may be broken by the user before delivery of the drug. Alternatively, a removable cap or the like may be provided over the nozzle. In one embodiment, the nozzle is provided with a twist-off plug which is broken from the nozzle by the user to open a passageway defined in the nozzle through which the drug may be delivered.

Thus, viewed from a further aspect the invention provides a nozzle for receiving a single dose of a pharmaceutical to be sealed therein and to form a capsule, the nozzle defining a passageway for delivery of the pharmaceutical and comprising means for closing off the passageway until the pharmaceutical is to be delivered.

In a preferred arrangement, the capsule is at least partially transparent such that the pharmaceutical is visible to a user from the outside of the capsule. In this way, it is possible for the user to check visually that the complete dose has been delivered and to repeat the drug delivery operation if necessary.

This, in itself, is believed to be a novel arrangement and thus viewed from a further aspect the invention provides a capsule comprising a single dose of a powdered pharmaceutical sealed within the capsule, wherein the capsule is at least partially transparent such that the delivery of the entire dose can be checked

visually by a user. Such a capsule may be arranged to be connected to a drug delivery device in such a manner that the contents of the capsule can be viewed before and after delivery.

In a preferred arrangement, the holder comprises a pump for urging the pharmaceutical through the nozzle. The pump may be of any suitable type, for example a squeeze bulb, a syringe pump or a rotary vane pump.

The pump may comprise a movable member that is resiliently biased by a spring, an elastic member or the like. The movable member may be movable to a priming position where it is held by a release mechanism, which is activated by the user to release the movable member to carry out a pumping movement. Advantageously, the movement associated with the connection of the capsule to the holder may also move the movable member to the priming position.

In general, the drug delivery device may be provided as a set comprising a holder and a plurality of capsules such that the same holder may be used with each of the capsules, each capsule being discarded after use.

The pharmaceutical may be in any suitable form, for example in the form of a fluid or liquid. In a preferred embodiment the pharmaceutical is in a particulate form, such as a powder, particles, granules, microballoons, microspheres, crystals, flakes or the like.

The device may be used to deliver the pharmaceutical to any externally voiding cavity of a human or non-human patient. Thus the device may be used for oral, pulmonary, sub-lingual, occular, anal, vaginal, aural or urethral delivery. In a preferred embodiment the device is used for nasal delivery of the pharmaceutical.

The capsule, in particular the nozzle, may be configured to provide a particular delivery pattern of the pharmaceutical to the patient. For example, the

nozzle may be configured to achieve a particular speed of delivery of the pharmaceutical or a particular geometry of the liquid or powder spray from the nozzle. In one arrangement, the diameter of the bore through which the pharmaceutical is delivered to the patient is selected to achieve the desired delivery speed. Such a bore may be narrow or wide and/or may be convergent or divergent towards the opening through which the pharmaceutical is delivered to the patient. The configuration of the nozzle may be selected by reference to the orifice into which the nozzle is intended to be applied and/or by reference to the type or form of the pharmaceutical.

Furthermore, the nozzle may comprise means for influencing the flow of air through the nozzle, for example to introduce turbulence into the flow and thereby ensure complete evacuation of the pharmaceutical or the creation of an effective aerosol.

The device may be used by the patient themselves or by a medical or veterinary practitioner or technician. In the case of drug delivery by such a person, the holder may be a more substantial device, for example provided with an electrically or pneumatically driven pump or connected to a source of compressed air or the like.

Some embodiments of the present invention will now be described, by way of example only, and with reference to the accompanying drawings, in which:

Figure 1 shows a drug delivery device according to an embodiment of the invention in a disassembled state;

Figure 2 is a sectional view corresponding to that of Figure 1;

Figure 3 shows the drug delivery device of Figure 1 in an assembled state and primed for drug delivery;

Figure 4 is a sectional view corresponding to that of Figure 3;

Figure 5 shows the drug delivery device of Figure 1

delivering a pharmaceutical;

Figure 6 is a sectional view corresponding to that of Figure 5;

Figure 7 shows a set comprising the drug delivery device of Figure 1 and a plurality of capsules;

Figure 8 shows, in section, an alternative embodiment of the capsule of the invention;

Figures 9a to 9d show, in section, configurations of the nozzle of the capsule according to embodiments of the invention;

Figures 10a to 10d show, in section, embodiments of the capsule according to the invention;

Figures 11a to 11c show, in plan, side and sectional views, flow directing devices for use in capsules according to embodiments of the invention;

Figures 12a to 12f show, in section, capsules according to embodiments of the invention incorporating the flow directing devices of Figures 11a to 11c;

Figures 13a to 13g illustrate the operation of a drug delivery device according to an alternative embodiment of the invention;

Figures 14a to 14g illustrate the operation of a drug delivery device according to a further embodiment of the invention; and

Figures 15a and 15b show, in section, a yet further embodiment of the device according to the invention.

In relation to the various embodiments of the invention, corresponding parts have been given corresponding reference numerals.

Referring to Figures 1 and 2, a drug delivery device 1 comprises a capsule 3 and a holder 5.

The capsule 3 is of molded plastics and is formed with a nozzle 7 which defines a container for a single dose of a pharmaceutical in powder form 9. The nozzle 7 is sealed at its tip by a plug 11 which can be twisted off the end of the nozzle 7 to leave an opening at the tip of the nozzle 7 through which the pharmaceutical 9

may be dispensed into the nasal passages of a patient.

The capsule 3 is provided with a bayonet connection 13 which engages with a complementary connection 15 on the holder 5 for attachment of the capsule 3 to the holder 5. In the region of the bayonet connection 13 the capsule 3 is provided with a frangible seal 17 of metal foil. When the complementary bayonet connections 13, 15 are interengaged, a piercing member 19 on the holder 5 penetrates the seal 17 to provide communication between the interior of the capsule 3 and the holder 5, via a passageway formed in the piercing member 19.

The holder 5 comprises a barrel 21 which receives a plunger 23 having a piston 25 at one end. The plunger 23 is biased towards the capsule-receiving end of the barrel 21 by a compression spring 27. The barrel 21 defines an opening in the region of its end opposite the capsule-receiving end, the opening receiving a button 29. The button 29 is the external element of a plunger-release mechanism which is arranged to engage the plunger 23 when the plunger 23 is retracted against the biasing force of the spring 27. The plunger-release mechanism retains the plunger 23 in the retracted position until the button 29 is depressed by the user. Depression of the button 29 releases the plunger 23 such that the spring 27 propels the plunger 23 rapidly towards the capsule 3. The movement of the plunger 23 causes the piston 25 to expel a jet of air through the passageway of the piercing member 19 into the capsule 3. In this way, the plunger 23 within the barrel 21 acts as a pump.

Figures 3 and 4 show the device 1 with the capsule 3 and holder 5 interconnected and the plunger 23 in the retracted position. The device 1 is thus primed for delivery of the pharmaceutical 9.

As shown in Figures 5 and 6, to dispense the pharmaceutical 9, the plug 11 is removed from the nozzle 7 and the nozzle 7 is inserted into the nostril of the

user (not shown). The button 29 is depressed, as indicated by arrow A, which causes the plunger 23 to move rapidly in the direction of arrow B, as described above. The jet of air passing into the capsule 3 from the holder 5 entrains the powdered pharmaceutical 9 and carries it out through the opening in the nozzle 7 in the form of an aerosol.

After the dose of pharmaceutical 9 has been delivered, the capsule 3 is detached from the holder 5 and disposed of. In a preferred arrangement, the capsule 3 is formed from transparent plastics so that the user can check visually that the entire dose has been delivered and re-prime and operate the device 1 if this is not the case.

Figure 7 shows a set comprising a plurality of capsules 3 and a single holder 5. The capsules 3 may each be used with the holder 5 as required and then disposed of. Although the set is shown with a separate case, it is also envisaged that the holder 5 may comprise means for storing a number of capsules.

It will be seen therefore that this embodiment of the invention provides a low-cost device which is very simple to use, requires no cleaning and provides complete protection of the drug from moisture and contamination.

Figure 8 shows an alternative embodiment of the capsule 3 according to the invention. In this embodiment, the pharmaceutical 9 is held between a first frangible seal 17 and a second frangible seal 31 which prevents the pharmaceutical 9 from exiting the capsule 3 until it is to be dispensed. In this embodiment, the twist-off plug 11 is not required.

In use, the capsule 3 is connected to the holder 5 and the piercing member 19 penetrates both seals 17,31 so that the pharmaceutical 9 can be dispensed in the manner described previously. In this way, the user is not required to twist-off the plug 11, which simplifies

operation of the device 1 for the user.

Figures 9a to 9d show embodiments of the capsule 3 according to the invention. In each of these embodiments, the nozzle 7 has a different internal profile, i.e. narrow bore (Figure 9a), divergent (Figure 9b), convergent (Figure 9c) and wide bore (Figure 9d). The narrow bore is between about 1 and 3 mm, preferably 2 mm, in diameter and the wide bore is greater than 3 mm, for example between 4 and 6 mm, preferably 5 mm in diameter. It has been found that each of these configurations imparts different characteristics to the plume of powder when it exits the nozzle 7. For example, it has been found that the wide bore configuration (Figure 9d) gives a powder plume with a low height due to energy losses within the bore combined with a low exit velocity. The presently preferred configuration is the narrow bore arrangement (Figure 9a), as this has a short, direct air path which encourages good evacuation with a small air volume, and has a powder plume with a wide spread. However, it may be that other configurations are preferred for particular applications because of the spatial and velocity profile that is required to achieve the necessary medical effect.

Figures 10a to 10d show each of the capsules 3 of Figures 9a to 9d in combination with a mesh filter 33 which supports the pharmaceutical 9 before delivery. The mesh filter 33 is held in position by a retaining ring 35 which engages with the interior surface of a widened portion of the interior of the nozzle 7.

The capsule 3 may comprise an air flow directing member 37, for example as shown in Figures 11a to 11c, to facilitate mixing of air and the pharmaceutical before delivery. The air flow directing member 37 is arranged in the air flow path between the holder 5 and the open end of the nozzle 7 and directs the air transversely to the direction of the flow path in order

to increase turbulence in the nozzle 7. Three exemplary air flow directing devices 37 are shown in Figures 11a to 11b. These are a cross-flow generating device (Figure 11a), a back flow generating device (Figure 11b) and a device (Figure 11c) which generates swirl about the longitudinal axis of the capsule 3. Figures 12a to 12f show these devices 37 in combination with the nozzle configurations shown in Figures 9c and 9d.

It will be apparent that the features of the capsules 3 shown in Figures 8 to 12 may be used in various combinations to achieve a capsule 3 suited to a particular application.

Figure 13 shows the operation of a device 1 according to an alternative embodiment of the invention. In this embodiment, the capsule 3 is provided with a cap 39, rather than the twist-off plug 11, which protects the nozzle 7 and the pharmaceutical 9, before the pharmaceutical is dispensed. The cap 39 is provided with a short rod 41 which projects into a hole defined in the nozzle 7 when the cap 39 is in place on the nozzle and thereby closes off the capsule 3.

A further feature of this embodiment is that the action of inserting the capsule 3 into the holder 5 is combined with the action of priming the syringe pump (not shown) in the holder 5. Thus, as shown in Figures 13a to 13g the user receives the holder 5 packaged together with two capsules 3 (Figure 13a). The user removes one capsule 3 from the package (Figure 13b) and applies the capsule 3 to the holder 5 (Figure 13c). The user pushes the capsule 3 into a hole defined in the holder 5 (Figure 13d) and this action connects the capsule 3 to the holder 5 and also primes the syringe pump (not shown) in the holder 5 so that, when the button 29 is pressed, the pump will activate to force a jet of air through the capsule 3. Once the pump has been primed by inserting the capsule 3, the cap 39 is removed from the capsule 3 (Figure 13e), and the user

inserts the nozzle 7 into the nostril (Figure 13f) and presses the button 29 to activate the pump and deliver the pharmaceutical 9. After use, the empty capsule 3 is discarded (Figure 13g).

Figures 14a to 14g illustrate a further embodiment of the device 1 according to the invention. In this embodiment, the capsule 3 is of a similar form to that described in relation to Figure 1. However, the pump in this case is a rotary vane pump, rather than a syringe pump, which is primed by pulling a priming member 43 into a priming position (see Figures 14b and 14c). The pump is activated by depressing the button 29, as shown in Figure 14e and the priming member 43 returns to its original position during activation of the pump, as shown in Figure 14f. Otherwise, the operation of the device 1 is similar to that of the embodiment of Figure 1.

Figure 15a shows a sectional view of a yet further embodiment of the invention. This embodiment differs from that shown in Figure 1 in that the pharmaceutical 9 is located in a passageway 45 defined in the capsule 3 and closed off at its ends by metal foil seals 17,31. As shown in Figure 15b, a further passageway 47 is defined in the holder 5. When the capsule 3 is connected to the holder 5, the seals 17,31 are broken by members (not shown) of the holder 5 and the two passageways 45,47 connect the barrel 21 of the holder to an airway 49 through the nozzle 7, so that the pharmaceutical 9 can be dispensed by a jet of air in a similar manner to that described in relation to the embodiment of Figure 1. The configuration of the capsule 3 and holder 5 with an S-bend according to this embodiment allows the capsule easily to be filled and closed using a single strip of metal foil. Furthermore, the S-bend arrangement prevents, to some extent, egress of the pharmaceutical 9 from the nozzle 7 once the seals 17,31 have been broken, if the connected capsule 3 and

holder 5 are inverted. It would be possible to add additional S-bends formed by communicating passageways in the capsule 3 and holder 5, to prevent totally the egress of the pharmaceutical 9 in this way.

It will be appreciated by those skilled in the art that the invention disclosed herein may be applied to embodiments other than that described above and that features described in relation to one embodiment may also be applied to the other embodiments disclosed herein.

Claims:

1. A capsule comprising a single dose of a pharmaceutical sealed within the capsule, characterised in that the capsule further comprises a nozzle for delivery of the pharmaceutical.

2. A capsule as claimed in claim 1 comprising a connector for connecting the capsule to a holder.

3. A capsule as claimed in claim 2, further comprising a frangible seal penetrable by a member of the holder.

4. A capsule as claimed in any preceding claim, comprising first and second frangible seals, wherein the pharmaceutical is contained between said seals.

5. A capsule as claimed in claim 4, wherein both of said seals are provided on one surface of the capsule.

6. A capsule as claimed in any preceding claim, comprising sealing means for sealing the nozzle.

7. A capsule as claimed in any preceding claim, wherein said capsule is at least partially transparent such that the pharmaceutical is visible to a user from the outside of the capsule.

8. A capsule as claimed in any preceding claim, comprising a device arranged to direct, in use, air flow through the capsule.

9. A drug delivery device comprising a capsule as claimed in any preceding claim and a holder.

10. A device as claimed in claim 9, wherein the holder comprises means for penetrating the capsule to allow

delivery of the pharmaceutical.

11. A device as claimed in claim 9 or 10, wherein the holder comprises a pump for urging the pharmaceutical through the nozzle.

12. A device as claimed in claim 11, wherein the holder is arranged such that, in use, the action of connecting the capsule to the holder also acts to prime the pump for delivery of the pharmaceutical.

13. A set comprising a device as claimed in any of claims 9 to 12 and at least one additional capsule as claimed in any of claims 1 to 8, wherein each of the capsules respectively is connectable to the holder for delivery of the pharmaceutical dose contained therein.

14. A nozzle for receiving a single dose of a pharmaceutical to be sealed therein and to form a capsule as claimed in any of claims 1 to 8, the nozzle defining a passageway for delivery of the pharmaceutical and comprising means for closing off the passageway until the pharmaceutical is to be delivered.

15. A capsule substantially as hereinbefore described with reference to the accompanying drawings.

16. A drug delivery device substantially as hereinbefore described with reference to the accompanying drawings.

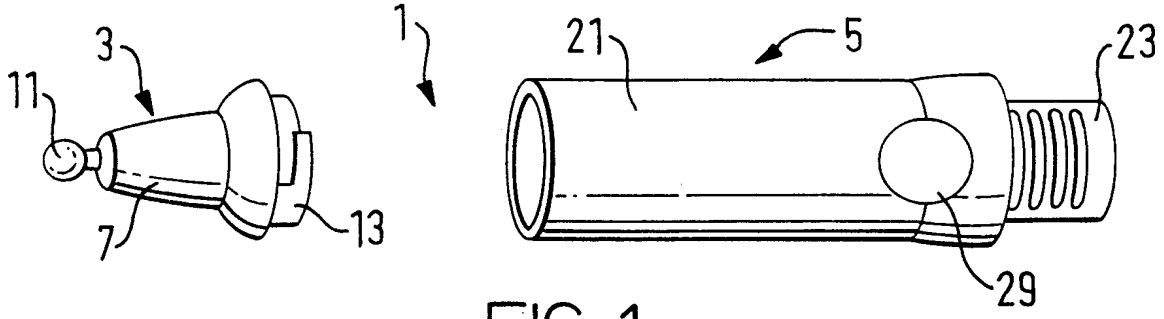


FIG. 1

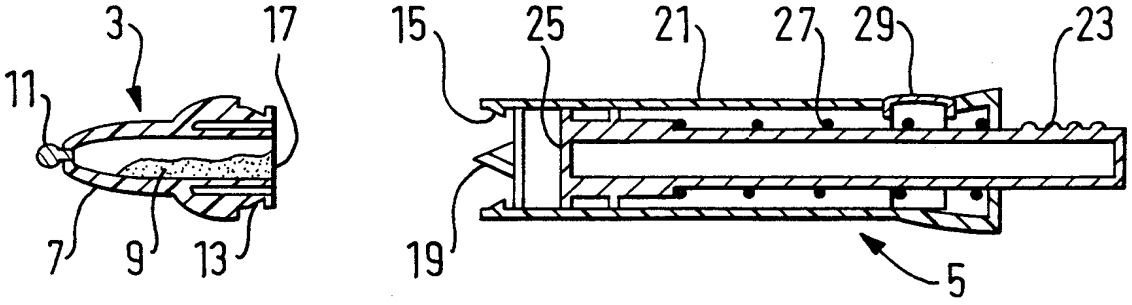


FIG. 2

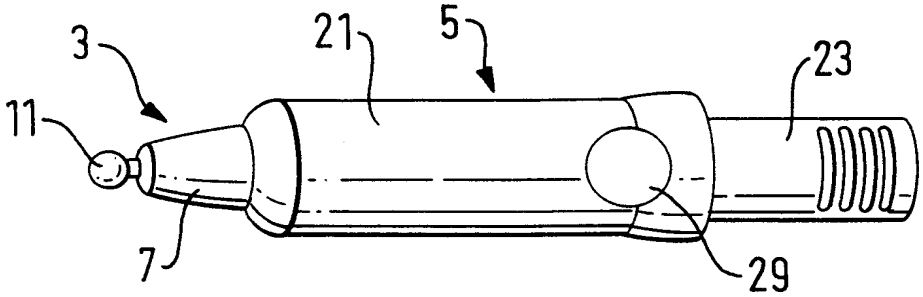


FIG. 3

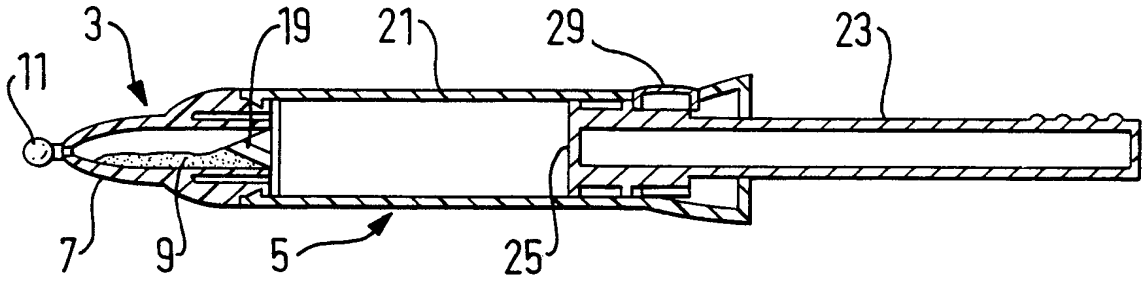


FIG. 4

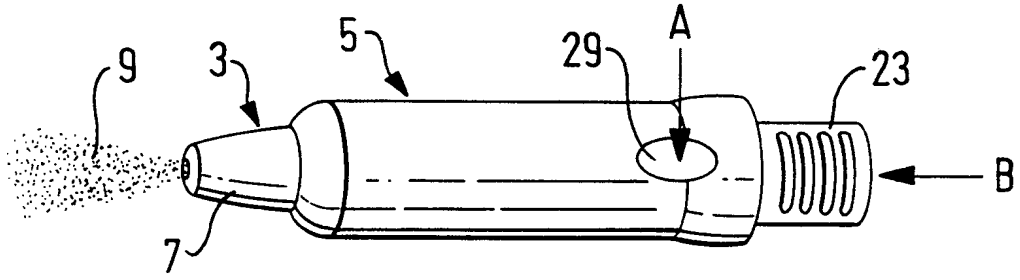


FIG. 5

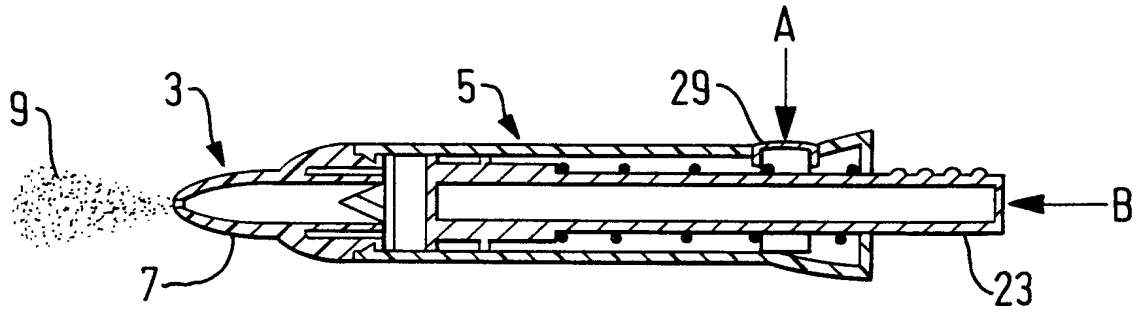


FIG. 6

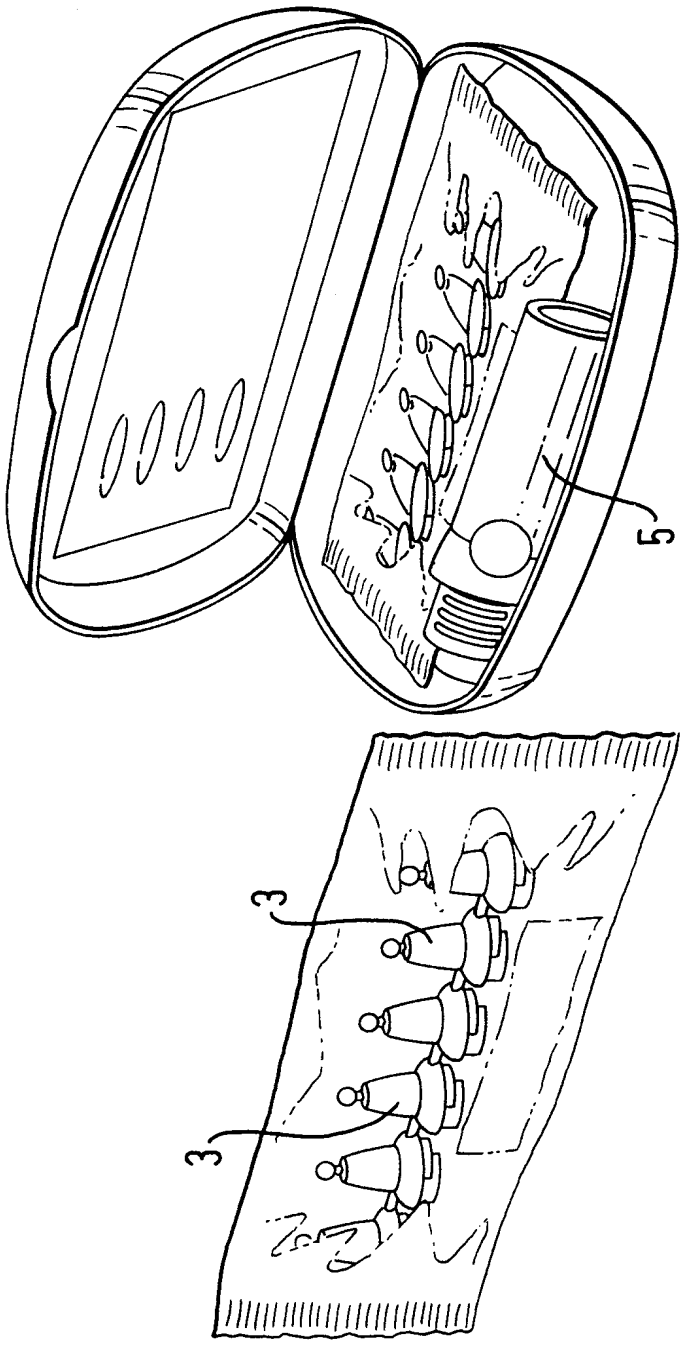


FIG.7

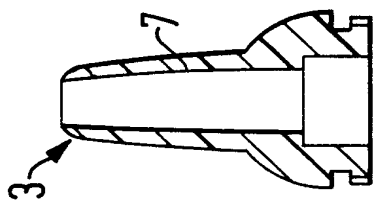


FIG.9d

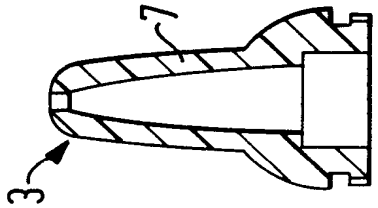


FIG.9c

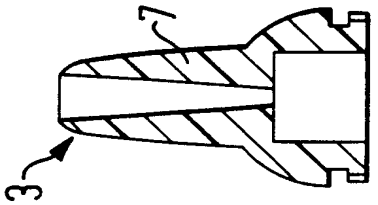


FIG.9b

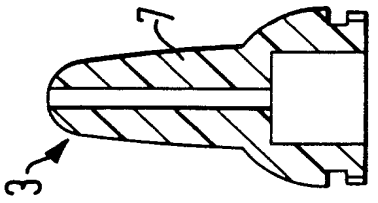


FIG.9a

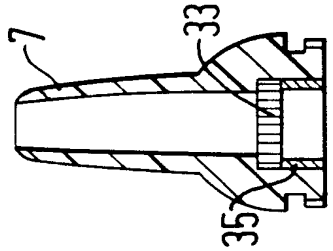


FIG.10d

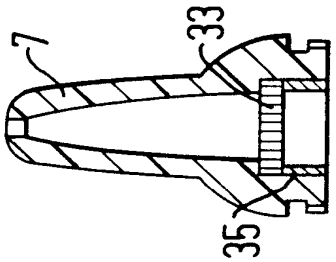


FIG.10c

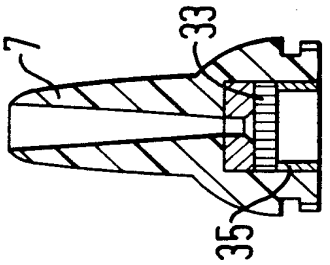


FIG.10b

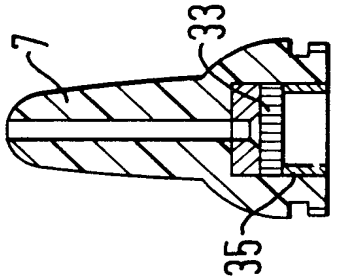


FIG.10a

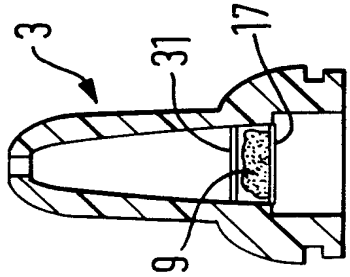


FIG.8

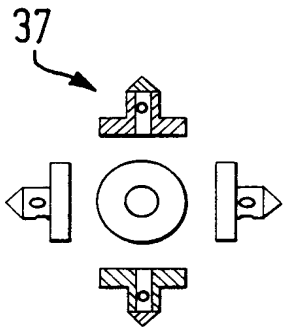


FIG.11a

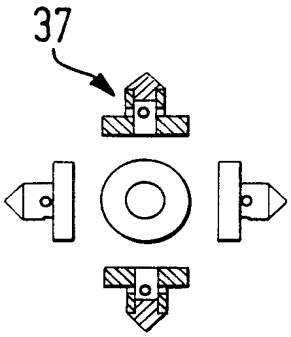


FIG.11b

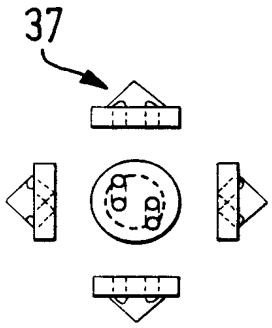


FIG.11c

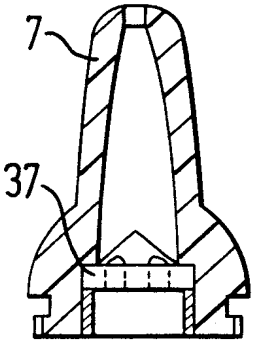


FIG.12a

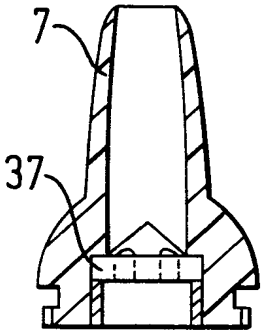


FIG.12b

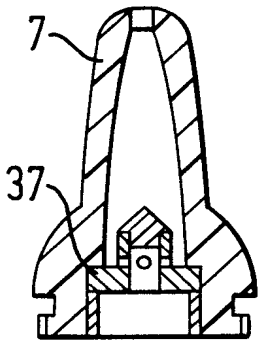


FIG.12c

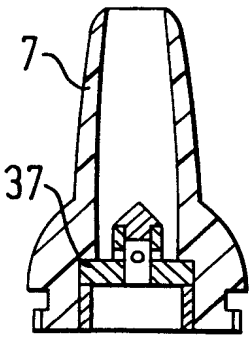


FIG.12d

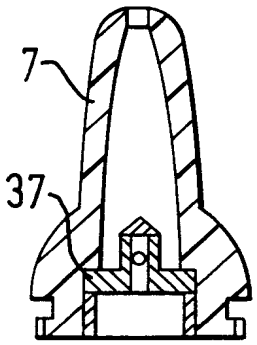


FIG.12e

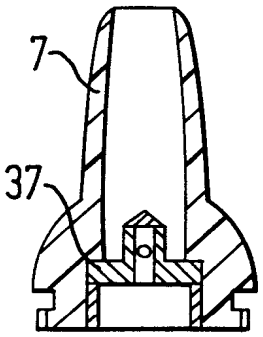


FIG.12f

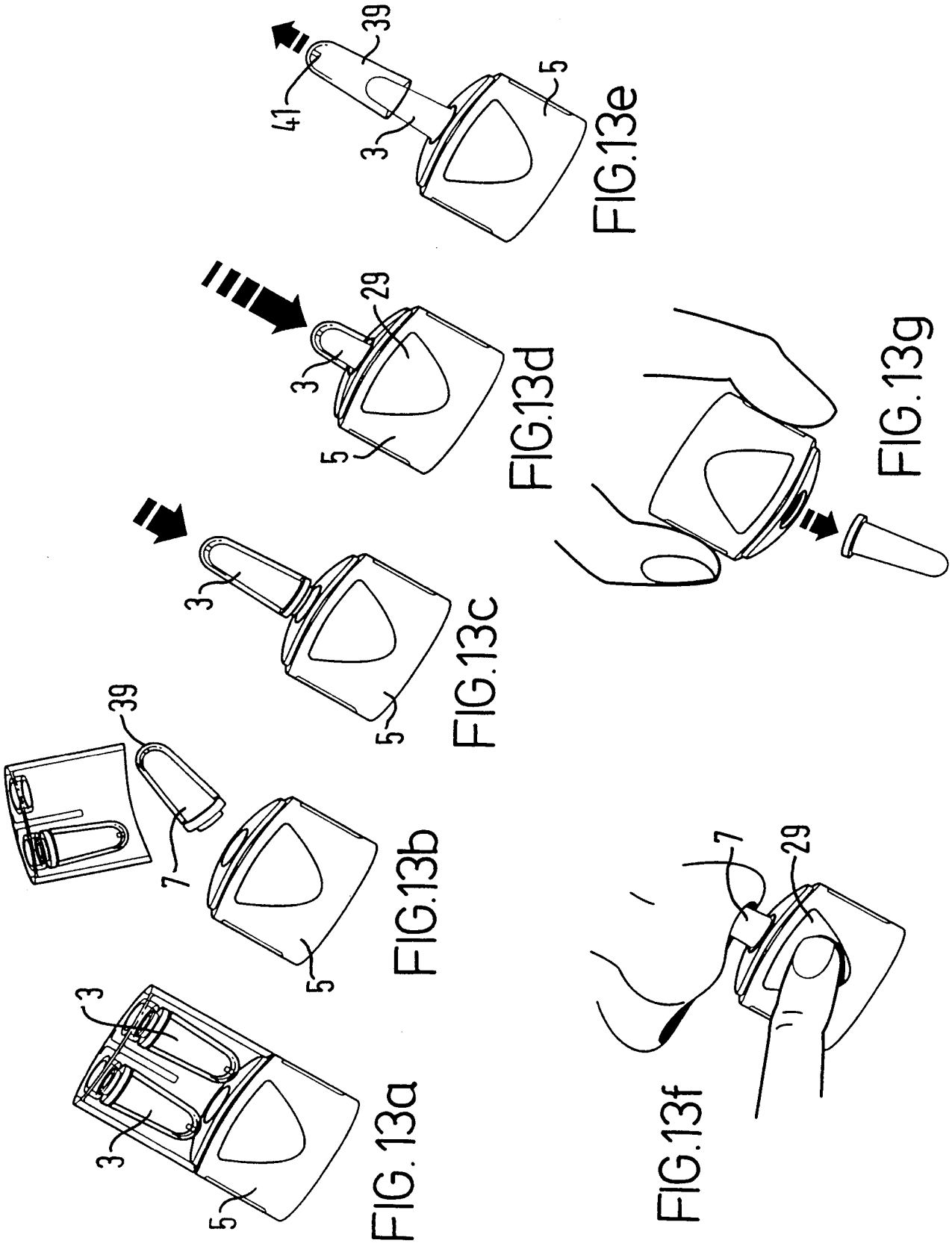
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FIG. 13a
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FIG.13b
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FIG.13c
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FIG.13d
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FIG.13e
FIG. 13g
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FIG.13f

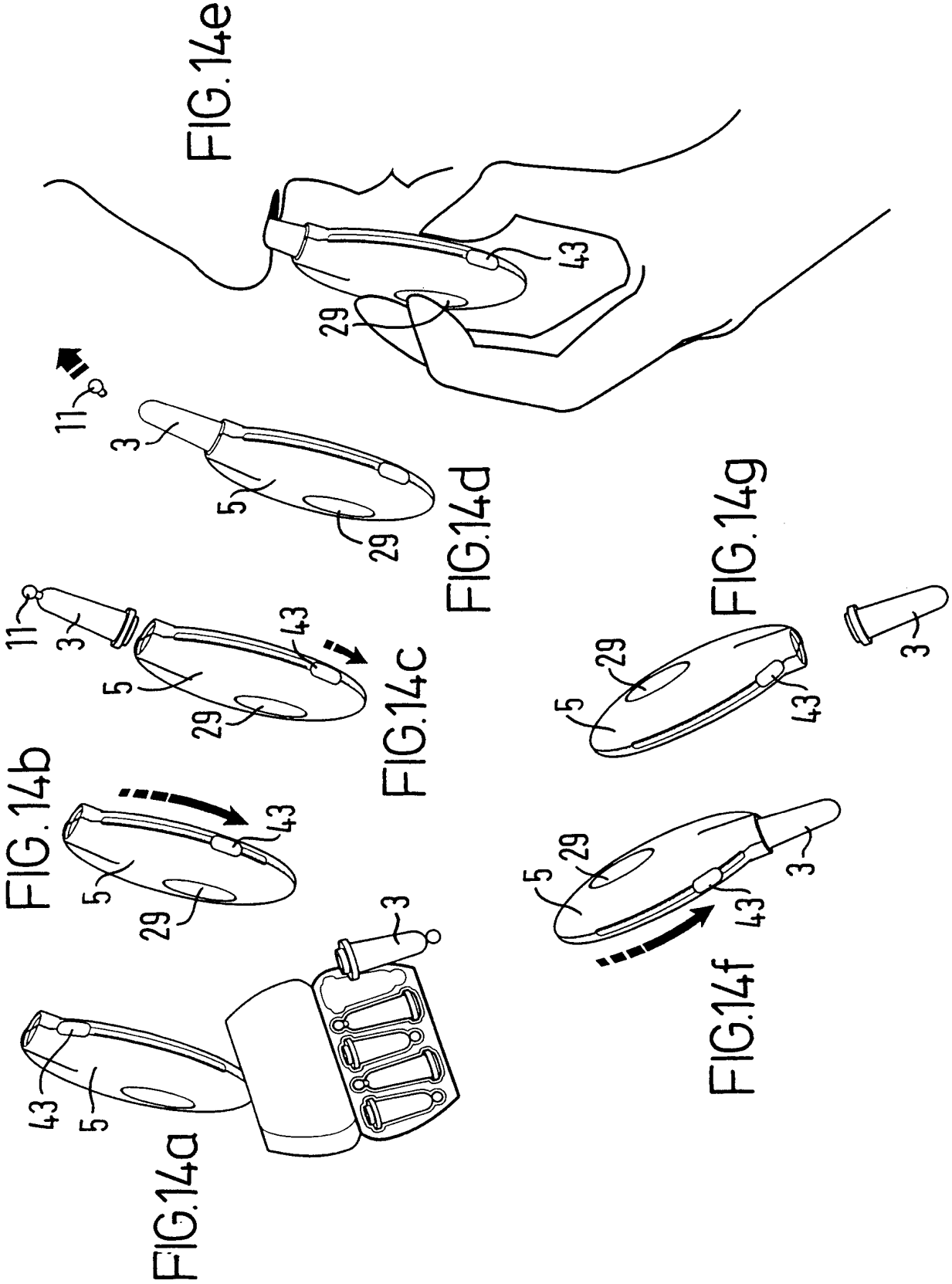
FIG.14e
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FIG14d
FIG.14b
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FIG.14c
FIG.14g
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FIG.14f
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FIG14a

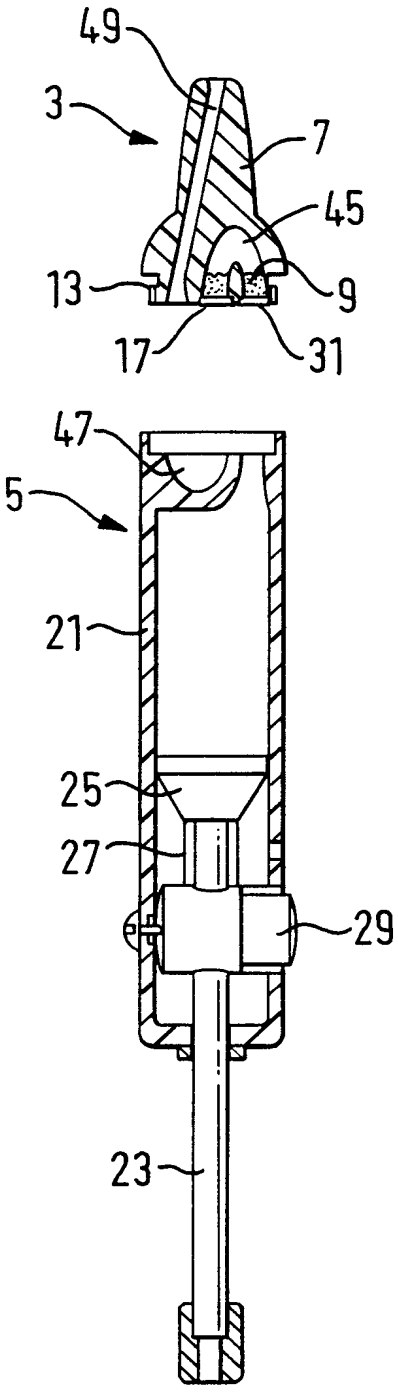


FIG.15a

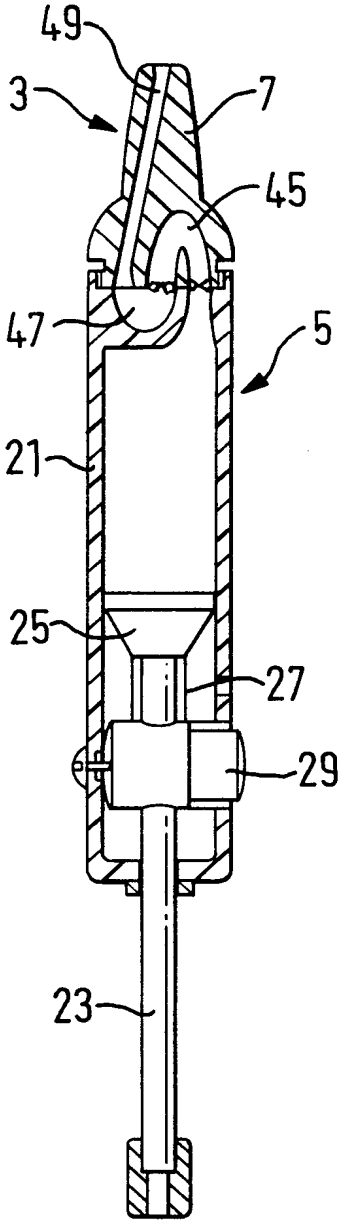


FIG.15b

# INTERNATIONAL SEARCH REPORT

Intern ial Application No
PCT/GB 99/01466

**A. CLASSIFICATION OF SUBJECT MATTER**
IPC 6 A61M15/08 A61M15/00

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X<br>A | US 2 519 555 A (M. R. FIELDS)<br>22 August 1950 (1950-08-22)<br>the whole document | 1-3,6,7,<br>9-11,14<br>13 |
| X | US 1 916 195 A (C. G. ANASTOR)<br>4 July 1933 (1933-07-04)<br>the whole document | 1,6-8,14 |
| X | WO 89 01348 A (TEIJIN LTD)<br>23 February 1989 (1989-02-23)<br>the whole document | 1,6,14 |
| X | EP 0 782 867 A (TEIJIN LTD)<br>9 July 1997 (1997-07-09)<br>page 8, line 1 - line 24; figures 1,2 | 1,6,14 |

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 9 August 1999 | 23/08/1999 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Jameson, P |

1

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# INTERNATIONAL SEARCH REPORT

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Inter ial Application No
PCT/GB 99/01466

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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| EP 0782867 A | 09-07-1997 | AU 703160 B | 18-03-1999 |
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| | | WO 9704826 A | 13-02-1997 |